

areas occurs when ICD is first detected. In agreement with a survival activity of Fgf8 on distal interdigital mesenchymal cells, inhibition of Fgf signaling prior to ICD initiation promotes cell death in this tissue. RA is necessary for ICD, since a RAR antagonist reduces ICD. Exogenous RA induces cell death in distal areas of the limb and exacerbates ICD, effect that can be reversed by exogenous Fgf8. In agreement with an antagonistic interaction between Fgf8 and RA, Fgf8 increases *Raldh2* and reduces *Cyp26b* expression, genes involved in the synthesis and degradation of RA, respectively; whereas, RA reduces Fgf8 expression. Surprisingly, ICD in the mouse does not require Bmp7, since noggin is unable to decrease ICD when applied in the interdigital regions. Noggin ectopic expression in the ectoderm reduces cell death and increases Fgf8 expression, suggesting an indirect regulation of ICD by Bmps. Our data indicate that the MAPK but not the PI3K pathway is used by Fgf8 to promote cell survival and expression of Mkp3.

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Program/Abstract # 442

Epithelial–mesenchymal interactions in hair follicle morphogenesis and regeneration

David Enshell-Seijffers, Catherine Lindon, Bruce A. Morgan
Cutaneous Biology Research Center, Harvard Medical School and Massachusetts General Hospital, Charlestown, MA, USA

The formation of hair follicles during embryogenesis and regeneration of follicles in the context of the hair cycle depend on inductive signaling between the epithelial and dermal components of the hair follicle. In particular, inductive signals from the dermal papilla (DP) are sufficient to drive follicle formation in competent epidermis and are thought to drive follicular regeneration during the hair cycle. While tools to manipulate gene expression in keratinocytes have allowed rapid progress towards characterizing these epithelial–mesenchymal interactions at the molecular level from the perspectives of the epithelium cells, the lack of tools to alter gene expression specifically in the DP has hampered progress towards defining the role of these cells. We have generated a mouse line that expresses the Cre recombinase specifically in the DP during the hair cycle. This line was employed to dissect the interaction between sonic hedgehog and wnt signaling in controlling specific aspects of DP activity. Activity of both pathways in the DP is required for normal morphogenesis of the hair shaft. While Wnt and Shh signaling act in concert for some aspects of hair morphogenesis, they appear to act in opposition on others.

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Early differentiation of uterine implantation zone in rats detected by a clearing technique

Luis A. Baiza-Gutman, Jaime Gómez-Jiménez
Unidad de Morfofisiología, FES-Iztacala, UNAM, Mexico

During pregnancy, uterine differentiation occurs in order to support embryo development. The earliest macroscopic uterine response to embryo signals is an increased vascular permeability detected after high molecular weight dye injection and known as blue reaction. Our aim was to analyze uterine macroscopic changes during early differentiation of implantation zones by a clearing procedure and its temporal relation with the vascular response to implantation. The uterus of Wistar rats of 3 to 7 days of gestation where cleared using hydrogen peroxide and benzylic alcohol, air was injected in the lumen before microscopic observation. The vascular response was detected by extravasation of Trypan blue. When we first detected the blue reaction on gestation day (GD) 5, a morphologically differentiated uterine zone of implantation (IZ) was clearly defined, the lumen was stretched, thinner and surrounded by a smooth surface of the uterine wall with an antimesometrial small invagination in the center of the zone (implantation chamber). Furthermore, at noon of GD 6 the lumen was dilated and at 18 h of day 6 the lumen was displaced to the mesometrial region, acquiring a horseshoe shape, the invagination in the center of IZ was more pronounced and decidualized area was present. In conclusion, the uterine wall and lumen experiment morphological changes simultaneously to vascular response during embryo implantation, which can be associated with increased vascular permeability, higher uterine hydration, fast proliferation of endometrial cells and decidualization.

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Peroxide mediates cell death during the formation of the proamniotic cavity

Leandro David Hernández-García, Susana Castro-Obregon, Concepción Valencia, Luis Covarrubias
Department of Develop. Genet. and Mol. Physiol., Instituto de Biotecnología/UNAM, Mexico

The formation of the proamniotic cavity is the first indication of programmed cell death associated to a morphogenetic process in mammals. Most what we know about proamniotic cavitation has come from studies done with embryoid bodies (EBs), structures derived from aggregation of embryonic stem (ES) cells. Reactive oxygen species (ROS) are potent activators of cell death, thus, in the present work we evaluated the role of ROS in EB cavitation. Before cavitation is completed, ROS concentration increases in the inner cells of EBs. EBs derived from ES cells that over-express the antioxidant enzyme catalase do not cavitate and